

CLAIMS

1. A pharmaceutical composition, said composition comprising a therapeutically effective amount of a compound of the formula R-COOH, or a salt or an ester or amide of such compound, where R designates a saturated or unsaturated alkyl chain of 10–24 carbon atoms, one or more of which may be replaced by heteroatoms, where one or more of said carbon or heteroatom chain members optionally forms part of a ring, and where said chain is optionally substituted by a hydrocarbyl radical, heterocyclyl radical, lower alkoxy, hydroxyl-substituted lower alkyl, hydroxyl, carboxyl, halogen, phenyl or (hydroxy-, lower alkyl-, lower alkoxy-, lower alkenyl- or lower alkinyl)-substituted phenyl, 10 C₃–C₇ cycloalkyl or (hydroxy-, lower alkyl-, lower alkoxy-, lower alkenyl- or lower alkinyl)-substituted C₃–C₇ cycloalkyl wherein said compound is capable of being endogenously converted to its respective coenzyme A thioester, RCOSCoA.

2. A composition according to claim 1, wherein R is selected from the group consisting of ω-carboxyl, ω-hydroxyl boron, and ω-hydroxyl chains.

3. A composition according to claim 1, where RCOOH is either clofibrlic acid or fibric acid, or a salt, ester, amide, or derivative thereof.

20 4. A composition according to claim 1, where RCOOH is a nonsteroidal antiinflammatory drug (NSAID).

5. A composition according to claim 1, where RCOOH is a saturated or unsaturated long chain fatty acid.

5 6. A composition according to claim 5, where the fatty acid is chosen from:

Stearic(18:0) acid
Oléic(18:1) acid
Linolenic(18:2) acid
Linolenic(18:3) acid
Eicosapentaenic(20:5) acid
Docosahexaenic(22:6) acid

7. A composition according to claim 1, wherein RCOOH is selected from the group consisting of:

1,16 Hexadecanedioic acid
1,18 Octadecanedioic acid
2,2,15,15-tetramethyl-hexadecane-1,16-dioic acid
2,2,17,17-tetramethyl-octadecane-1,18-dioic acid
3,3,14,14-tetramethyl-hexadecane-1,16-dioic acid
20 3,3,16,16-tetramethyl-octadecane-1,18-dioic acid
4,4,13,13-tetramethyl-hexadecane-1,16-dioic acid and
4,4,15,15-tetramethyl-octadecane-1,18-dioic acid

25 8. A composition according to claim 1, wherein RCOOH is selected from the group consisting of:

16-B(OH)2-hexadecanoic acid
18- B(OH)2-octadecanoic acid
16- B(OH)2-2,2-dimethyl-hexadecanoic acid

18- B(OH)2-2,2-dimethyl-octadecanoic acid
16- B(OH)2-3,3-dimethyl-hexadecanoic acid
18- B(OH)2-3,3-dimethyl-octadecanoic acid
16- B(OH)2-4,4-dimethyl-hexadecanoic acid
5 18- B(OH)2-4,4-dimethyl-octadecanoic acid

9. A composition according to claim 1, wherein RCOOH is selected from the group consisting of:

10 16-hydroxy-hexadecanoic acid
18-hydroxy-octadecanoic acid
16-hydroxy-2,2-dimethyl-hexadecanoic acid
18-hydroxy-2,2-dimethyl-octadecanoic acid
16-hydroxy-3,3-dimethyl-hexadecanoic acid
18-hydroxy-3,3-dimethyl-octadecanoic acid
15 16-hydroxy-4,4-dimethyl-hexadecanoic acid
18-hydroxy-4,4-dimethyl-octadecanoic acid

10 10. A method of treating an HNF-4 mediated disease state which method comprises administering a therapeutically effective amount of a compound which
20 inhibits HNF-4 controlled transcription.

11. A method of claim 10 wherein said compound comprises an amphipathic carboxylate capable of being converted to its respective CoA thioester.

25 12. A method of claim 11 wherein said amphipathic carboxylate is a xenobiotic amphipathic carboxylate.

13. A method of claim 10 wherein said compound shifts the HNF-4 dimer-oligomer equilibrium to favor an oligomer.

5 14. A method of claim 10 wherein said compound decreases the binding affinity of the HNF-4 dimer for a target gene.

10 15. A method of claim 11 wherein said amphipathic carboxylate is a C18:3 fatty acid.

16. A method of claim 11 wherein said amphipathic carboxylate is a C20:5 fatty acid.

17. A method of claim 10 for the treatment of Syndrome X.

15 18. A method of claim 10 for the treatment of coronary or peripheral atherosclerosis.

19. A method of claim 10 for the treatment of rheumatoid arthritis, multiple sclerosis, psoriasis or inflammatory bowel diseases.

20 20. A method of claim 10 for the treatment of breast cancer, colon cancer or prostate cancer.

21. A method of modulating HNF-4 transcriptional activity in vivo comprising exposing the HNF-4 or a nucleic acid encoding HNF-4 to an effective amount of an amphipathic carboxylate, an antisense molecule, a ribozyme, or an antibody for HNF-4 or its gene.

5 22. A method of claim 21 wherein said amphipathic carboxylate is a fatty acid capable of being converted to its respective CoA thioester.

23. A method of claim 21 wherein said modulation is inhibition of HNF-4 activity.

24. A method of claim 21 wherein said modulation is activation of HNF-4 activity.

10 25. A method of claim 21 wherein said amphipathic carboxylate is a C18:3 fatty acid.

26. A method of claim 21 wherein said amphipathic carboxylate is a C20:5 fatty acid.

15 27. A method of claim 21 wherein the modulation is via antibody interaction.

28. A method of claim 10 wherein said compound is an antisense molecule, a ribozyme, or an antibody to HNF-4.